

AMENDMENT(S) TO THE SPECIFICATION

Please replace the paragraph at column 1, lines 9-15 of U.S. Patent 6,440,392, with the following rewritten paragraph:

1. Field of the Invention

The present invention relates to [an] intranasal pharmaceutical compositions comprising calcitonin as an active ingredient and specific concentrations of citric acid or a salt thereof as a stabilizer and absorption enhancer.

Please replace the paragraph at column 1, lines 24-47 of U.S. Patent 6,440,392, with the following rewritten paragraph:

Given their size and chemical composition, calcitonins were originally administered by subcutaneous or intramuscular injection. Other routes of administration were technically difficult because calcitonins were poorly absorbed through tissue and were readily degraded by bodily fluids. Despite these obstacles, a formulation (U.S. Patent 5,759,565) was developed that could be administered via the nasal route. The nasal formulation was designed to be stored in a multi-dose container that was stable for an extended period of time and resisted bacterial contamination. The preservative in the formulation, benzalkonium chloride, was found to enhance the absorption of salmon calcitonin. However, benzalkonium chloride was reported (P. Graf et al., Clin. Exp. Allergy 25:395-400; 1995) to aggravate [rhinitis] rhinitis medicamentosa in healthy volunteers who were given a decongestant nasal spray containing the preservative. It also had an adverse effect on nasal mucosa (H. Hallen et al., Clin. Exp. Allergy 25:401-405; 1995). Berg et al. (Laryngoscope 104:1153-1158; 1994) disclose that respiratory mucosal tissue that was exposed *in vitro* underwent severe morphological alterations. Benzalkonium chloride also caused significant slowing of the mucociliary transport velocity in the *ex vivo* frog palate test (P.C. Braga et al., J. Pharm. Pharmacol. 44:938-940; 1992).

Please replace the paragraph at column 3, lines 15-20 of U.S. Patent 6,440,392, with the following rewritten paragraph:

The compositions of the invention should also possess an appropriate isotonicity and viscosity. Preferably they have an osmotic pressure of from about 260 to about 380 mOsm/liter. Desired viscosity for the nasal spray is preferably less than 0.98 cP. In one embodiment, the osmotic pressure is from 250 to 350 mOsm/liter.

Please replace the paragraph at column 4, lines 44-50 of U.S. Patent 6,440,392, with the following rewritten paragraph:

In single-dose studies, blood samples are collected prior to dosing and at 5, 15, 30, 60 and 120 minutes after dosing. In multiple-dose studies, blood samples are collected prior to dosing and at 30, 60, 90, 120 and 150 minutes after the administration of the first dose. Blood samples are always collected immediately before the administration of any additional [costs] doses.